Atty. Dkt. No. 036481-0135

*IN THE UNITED STATES PATENT AND TRADEMARK OFFICE*

Applicant: Joel R. HAYNES et al.

Title: ADJUVANTED GENETIC VACCINES

Appl. No.: 09/433,777

Filing Date: November 3, 1999

Examiner: A. M. S. Wehbe

Art Unit: 1632

**PETITION FOR WITHDRAWAL OF HOLDING OF ABANDONMENT UNDER 37 C.F.R. § 1.181(b)**

Mail Stop PETITION
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

This Petition is in reply to the Notice of Abandonment mailed September 9, 2003. Applicants hereby petition for withdrawal of the holding of abandonment. Applicants also include herewith a copy of the executed Associate Power of Attorney that is being filed with the USPTO concurrently with this Petition (APPENDIX A).

In response to the final Office Action dated August 13, 2002, attached hereto as APPENDIX B, Applicants filed a Notice of Appeal on January 13, 2003, with a two-month extension of time. The Notice of Appeal with two-month extension of time is attached as APPENDIX C. On July 8, 2003, Applicants then hand-deposited a Request for Continued Examination, a *bona fide* reply to the final Office Action, and an Information Disclosure Statement, along with the appropriate petition for extension of time and fees to make the July 8th submission timely. Copies of these documents are attached as APPENDIX D.

Applicants received in return a date-stamped notification from the Patent Office evidencing that these papers had in fact been received by "TECH CENTER 1600/2900" on

July 8, 2003, at 8 pm. The notification also was marked with an "ENTERED" stamp and is attached as APPENDIX E.

However, Applicants next received from the Office a Notice of Abandonment on September 9, 2003, indicating that "no reply [to the August 13, 2002 Action] has been received" (APPENDIX F).

Of course, this is incorrect, and in view of the foregoing, Applicants request that the PTO withdraw the holding of abandonment of this application and return the application to pending status.

Since this Petition is being filed within two months of the mailing date of the Notice of Abandonment, Applicants submit that the Petition is timely under 37 C.F.R. § 1.181(a). No fee is believed to be due, but the Commissioner is authorized to charge any deficient fees, or credit any overpayment, to Deposit Account No. 19-0741. See MPEP 711.03(c) sec. I.

Applicants also would like to point out that the Attorney Docket Number reference for this application has changed, from "APF-18.20" to "036481/0135." The Examiner is invited to contact the undersigned by phone to expedite this process.

Respectfully submitted,

Date October 24, 2003

By Richard C Peet

FOLEY & LARDNER
Customer Number: 27476
Telephone: (202) 672-5483
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Richard C. Peet
Attorney for Applicant
Registration No. 35,792

Atty Dkt APF 18.20
PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on _____.

_____ _____
Date Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Serial No.: 09/433,777 Art Unit: 1632
Filing Date: 03 Nov 1999 Examiner: A.M.S. WEHBE

Title: Adjuvanted Genetic Vaccines

**ASSOCIATE POWER OF ATTORNEY**
**UNDER 37 C.F.R. § 1.34**

Commissioner for Patents
Washington, D.C. 20231

Sir:

I, the undersigned attorney of record in the above-referenced patent application, do hereby grant associate power of attorney to prosecute this application and any continuations, divisions, reissues and reexaminations thereof, and transact all business in the United States Patent and Trademark Office connected therewith, to the following registered attorneys and agents:

Alisa A. Harbin, Reg. No. 33,895;
the registered attorneys and agents of Foley & Lardner at Customer Number 23524;
Richard C. Peet, Reg. No. 35,792;
Jayme Huleatt, Reg. No. 34,485;
Frederic Tenney, Reg. No. 47,131;
Amy Rocklin, Reg. No. 47,033;
Alison Scheidler, Reg. No. 54,425;
Eve Frank, Reg. No. 46,785;

Robert P. Blackburn, Reg. No. 30,447;
Joseph H. Guth, Reg. No. 31,261;
Charlene A. Launer, Reg. No. 33,035;
Rebecca M. Hale, Reg. No. 45,680;
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Gerald Suh, Reg. No. 41,337.

Please address all future correspondence relating to this application to:

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Respectfully submitted,

By: 

Thomas P. McCracken
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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
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www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/433,777 | 11/03/1999 | JOEL R. HAYNES | APF-18.20 | 2990 |

7590 09/09/2003

THOMAS P MCCRACKEN
POWDERJECT TECHNOLOGIES INC
Florey House, Oxford Science Park
Oxford, ENG 94555
UNITED KINGDOM

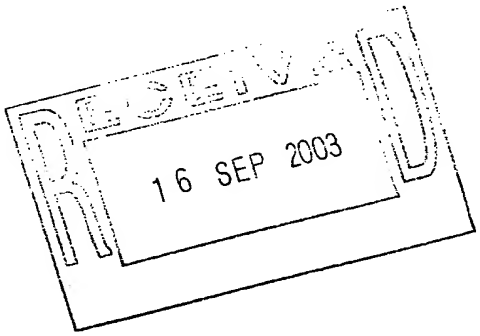
AIR MAIL

| EXAMINER |
|---|
| WEHBE, ANNE MARIE SABRINA |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.



| Notice of Abandonment | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/433,777 | HAYNES ET AL. | |
| | Examiner | Art Unit | |
| | Anne Marie S. Wehbe | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--*

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on *13 August 2002*.
   (a) ☐ A reply was received on _____ (with a Certificate of Mailing or Transmission dated _____ ), which is after the expiration of the period for reply (including a total extension of time of _____ month(s)) which expired on _____.
   (b) ☐ A proposed reply was received on _____, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection.
   (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
   (c) ☐ A reply was received on _____ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
   (d) ☒ No reply has been received.

2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
   (a) ☐ The issue fee and publication fee, if applicable, was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
   (b) ☐ The submitted fee of $_____ is insufficient. A balance of $_____ is due.
   The issue fee required by 37 CFR 1.18 is $_____. The publication fee, if required by 37 CFR 1.18(d), is $_____.
   (c) ☐ The issue fee and publication fee, if applicable, has not been received.

3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
   (a) ☐ Proposed corrected drawings were received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply.
   (b) ☐ No corrected drawings have been received.

4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.

5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.

6. ☐ The decision by the Board of Patent Appeals and Interference rendered on _____ and because the period for seeking court review of the decision has expired and there are no allowed claims.

7. ☐ The reason(s) below:

ANNE M. WEHBE
PRIMARY EXAMINER

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

Exp. 1410
CM 17

***RECEIVED BY THE UNITED STATES PATENT AND TRADEMARK OFFICE***

03 JUL -0 PM 12:27

RECEIVED
TECH CENTER 1600/2900

***ATTORNEY DOCKET***: APF 18.20

***PAPERS***: Request for Continued Examination (RCE) Transmittal (2 sheets); Petition for Extension of Time (1 sheet); Communication (12 sheets); Information Disclosure Statement (4 sheets); Form PTO-1449 (3 sheets); and copies of 30 cited references.

***APPLICANT***: HAYNES et al.
***SERIAL NUMBER:*** 09/433,777
***FILING DATE:*** 3 November 1999

ENTERED

***DATE RECEIVED BY USPTO:*** _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Washington, D.C. 20231
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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/433,777 | 11/03/1999 | JOEL R. HAYNES | APF-18.20 | 2990 |

7590 08/13/2002

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UNITED KINGDOM

AIR MAIL

| EXAMINER | |
|---|---|
| WEHBE, ANNE MARIE SABRINA | |
| ART UNIT | PAPER NUMBER |
| 1632 | |

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/433,777 | HAYNES ET AL. | |
| | Examin r | Art Unit | |
| | Anne M Wehbé | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the corr spond nce address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *6,8-11,13,14 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,12,15-25 and 29-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicant's response received on 6/7/02 has been entered. Claims 27-28 have been canceled. Claims 1-26 and 28-47 are pending in the instant application. Of these, claims 6, 8-11, 13-14, and 26 have been withdrawn from consideration as being drawn to subject matter non-elected without traverse in paper no. 7. Please note that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-5, 7, 12, 15-25, and 29-47 are therefore under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

### *Claim Rejections - 35 USC § 112*

The rejections of claims 27 and 28 under 35 U.S.C. 112, second paragraph, and 35 U.S.C. 101 are withdrawn in view of applicant's cancellation of the claims

The rejection of pending claims 1, 16, and 29-47 under 35 U.S.C. 112, first paragraph, for lack of enablement is maintained over claims 1, 16, and 33-47. Applicant's arguments have

been fully considered but have not been found sufficient in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the rejection of record focuses on one embodiment of the claimed invention, wherein the claimed compositions include an "immune shift lipid adjuvant", and that the office has not given sufficient weight to applicant's working examples which utilize non-lipid adjuvants. In response, please note that the applicant has previously elected the species of "lipid adjuvants" for prosecution in the instant application. Further, the rejection of record is concerned with the lack of enablement provided by the specification for shifting the immune response from Th1 to Th2 or vice versa using any lipid adjuvant. This rejection does not state that the specification is not enabling for method of generating immune responses to antigen using the disclosed compositions of DNA and non-DNA lipid adjuvants. The rejection of record is specifically concerned with the lack of enablement for using lipid adjuvants with are capable of "shifting" the immune response. The applicant has defined the term "immune shift" as meaning a shift in the immune response from a Th1 response to a Th2 response or vice versa, see specification page 14, lines 19-27. Therefore, by the applicant's own definition of the term, claims reciting an "immune shift" require more than simply generating or enhancing an immune response to an antigen. The term "immune shift" has patentable weight in the claims in terms of enablement, and is particularly claimed in claims 16, and 33-47. Claim 1 has been included in this rejection as claim 16 depends on claim 1. As such, it is proper to consider whether the

specification provides an enabling disclosure for this particularly claimed limitation of the instant invention.

The applicant further argues that the previous office action focused on the results obtained in the specification working example which uses MPL adjuvant combined with DNA encoding a CEA antigen, and does not take into account applicant's working examples which utilize antigens from HIV or hepatitis B in combination with Quil A. Please note that the applicant has elected the species of "lipid" adjuvants for prosecution in the instant application. Quil A is a saponin adjuvant, not a lipid adjuvant. Therefore, data regarding the use of Quil A as the non-DNA adjuvant concerns subject matter non-elected in the instant application. The issue at hand is whether the specification provides an enabling disclosure for lipid based adjuvants. Thus, the relevant working example in the specification is the working example where the applicants tested compositions comprising monophosphoryl lipid A and DNA encoding CEA. The previous office action analyzed the working example which uses a lipid adjuvant as follows. The specification provides a working example of the instant invention which demonstrates that co-administration of gold beads coated with monophosphoryl lipid A (MPL) and gold beads coated with a DNA plasmid vector encoding the carcinoembryonic antigen (CEA) under transcriptional control of the CMV promoter to the epidermis of Balb/C mice by particle-mediated bombardment results in a decrease in the ratio of CEA specific IgG1 to IgG2a in mouse serum compared to the administration of CEA-plasmid alone. The specification provides no data concerning the T helper cytokine patterns or level of anti-CEA cytotoxicity in the vaccinated mice. The specification suggests that this

decrease in the IgG1/IgG2a ratio correlates to a shift in the T helper phenotype of the mouse's immune response to CEA from a Th2 to a Th1 type response. However, it is clear that the applicant's data does not demonstrate a "shift" from Th2 to Th1 since the overall ratio of IgG1 to IgG2a shows that the predominant isotype is IgG1 rather than IgG2a which indicates a Th2 type response. The applicant's data therefore only demonstrates a decrease in the magnitude of the T helper response rather than an actual shift. Thus, the skilled artisan would not find the specification's working example evidence that the co-administration of MPL shifts the immune response generated against CEA from a Th2 type response to a Th1 type response as the mice continue to exhibit primarily IgG1 anti-CEA antibodies. The applicant has not refuted these findings.

In regards to applicant's argument that the working examples utilize an art-recognized mouse model and that human clinical data is not required, please note that the previous office action did not require human clinical data and did **not** state that the mouse model was not suitable for exemplifying immunological compositions. The applicant has misunderstood the grounds of rejection. The previous office action explained in some detail that T helper subsets have not been fully characterized for any species other than mouse, and that it was clearly known in the prior art at the time of filing that different strains of inbred mice appeared to respond differently to antigens in terms of the generation of Th1 versus Th2 responses (Golding et al., Abbas et al.). In analyzing the applicant's working example, the office simply pointed out that the applicant's working example where Balb/C mice were injected with gold beads coated with monophosphoryl lipid A

and a plasmid encoding CEA did not in fact demonstrate any actual "immune shift" from Th1 to Th2, and that based on the known differences in T helper responses to antigen observed in different strains of mice, the skilled artisan would not have been able to predict whether monophosphoryl lipid A would be capable of causing an "immune shift" to an antigen in any species of mouse or other mammals.

In regards to the applicant's argument that the office has not met its burden to provide a reasonable basis to question the enablement of the instant specification for the elected subject matter, citing *In re Wright* and *In re Marzocchi*, it is noted that the previous office action analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, and 5) the presence or absence of working examples, and presented detailed scientific reasons supported by publications from the prior art for the finding of a lack of enablement in the instant. Further, case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Finally, the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991).Therefore, due to the art recognized complexity and unpredictability of shifting the T helper immune response to a pathogenic antigen in mammals, the breadth of the claims, and the lack of sufficient guidance from the specification concerning vector

and promoter selection, level of antigen expression, genetic background of the mammal to be vaccinated, and routes of administration in regards to their affect on a) generating a particular T helper response in the absence of adjuvant and b) the ability of a particular lipid adjuvant to shift that T helper response to either Th1 or Th2, it would have required undue experimentation to practice the invention as claimed.

***Claim Rejections - 35 USC § 102***

The rejection of pending claims 1-2, 7, 12, 15, 27-29, 33, 35, 37, 39, 41, 43, and 46-47 under 35 U.S.C. 102 (e) as being anticipated by U.S. Patent No. 5,925,362, hereafter referred to as Spitler et al., is maintained. Applicant's arguments have been fully considered but have not been found sufficient in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the office has misconstrued the teachings of Spitler et al. The applicant states that in columns 7-9 of the Spitler et al. patent, the disclosure refers to the combination of protein/peptide PSA antigens and liposomal adjuvants, and does not actually teach the combination of nucleic acid sequences encoding PSA in combination with non-DNA adjuvants. Based on applicant's analysis of the Spitler specification, the applicant concludes that Spitler never contemplated applicant's claimed combination of nucleic acid and non-DNA adjuvant. This interpretation of the teachings of Spitler et al. is clearly incorrect. Claim 1 of the

Spitler patent recites a method of eliciting an antitumor immune response to prostate tumors in a subject comprising administering to said subject an active ingredient comprising either human PSA, or an expression system capable of generating in situ said human PSA. Claim 5, which depends on claim 1, clearly recites wherein the active ingredient is formulated to be encapsulated in a liposome or coupled to a liposome and wherein said liposomes optionally contain an adjuvant. Claim 6 also recites the method of claim 1 which further includes at least one adjuvant capable enhancing said antitumor immune response. Claim 7, which depends on claim 6, recites a list of adjuvants which include monophosphoryl lipid A. Since the claims clearly recite the combination of **either** a protein PSA antigen or an expression system capable of generating in situ said PSA and an adjuvant such as monophosphoryl lipid A, there can be no doubt that Spitler et al. contemplated applicant's claimed combination of nucleic acid encoding an antigen and non-DNA adjuvant. Furthermore, contrary to applicant's analysis of the teachings of columns 7-8, column 8, lines 9-12, clearly states that as an embodiment of the instant invention recombinant vectors included in a liposome injectable "as described above" can be administered to the subject. The description of liposome injectables referenced in column 8 can be found in column 7 which clearly teaches that liposomes may also include immune system adjuvants such as lipid A. Thus, it is clear from both the teachings of the specification and the claims of the 5,925,362 patent, that Spitler et al. teaches all the elements of the applicant's invention. As such, Spitler et al. anticipates the invention as claimed.

Please note as well that the previous office action stated that while Spitler et al. does not specifically teach that monophosphoryl lipid A "shifts" the immune response to PSA, case law states that "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). The applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

***Claim Rejections - 35 USC § 103***

The rejection of claims 1, 3-5, 17-25, 29-34, 36-38, 40, 42, 44-45 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,925,362, hereafter referred to as Spitler et al., in view of Fynan et al., Golding et al., and Sedegah et al. is maintained. Applicant's arguments have been fully considered but have not been found sufficient in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the office has not met the requirements set forth in section 2143 of the MPEP for establishing *prima facie* obviousness over the applicant's claimed invention. The applicant's reason for this conclusion is based on applicant's contention that the primary reference Spitler et al. does not teach or suggest applicant's claimed combination of a DNA encoding an antigen and a non-DNA adjuvant. The applicant has not provided any actual arguments traversing the teachings of Fynan, Golding, or Sedegah as applied in the instant rejection. The applicant's arguments concerning the teachings of Spitler et al. are discussed in detail above in the response to applicant's arguments concerning the teachings of Spitler et al. under 35 U.S.C. 102(e). In brief, the office finds that in particular claims 1, and 5-7 of the Spitler et al. patent clearly recite the combination of an expression system encoding a PSA antigen and a non-DNA adjuvant such as monophosphoryl lipid A for use in generating anti-tumor immune responses in vivo in a subject. Therefore, the office submits that the previous office action did in fact follow the three basic requirements for *prima facie* obviousness as required by section 2143 of the MPEP.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

Anne-marie Baker

ANNE-MARIE BAKER
PATENT EXAMINER

POWDERJECT
PHARMACEUTICALS PLC

| | |
|---|---|
| **Fax To:** | Examiner Anne Marie Sabrina Wehbe<br>United States Patent and Trademark Office<br>Group Art Unit 1632 – BOX AF |
| **Fax Nº:** | **(703) 308-4242** |
| **From:** | Thomas P. McCracken |
| **Date:** | 13 January 2003 |
| **Re:** | **Patent Application Serial No. 09/433,777** |
| **Pages:** | 3 (including this one) |

**Please deliver the attached documents (Petition for Extension of Time and Notice of Appeal), totaling with this cover sheet 3 pages, to Examiner Anne Marie Sabrina Wehbe of Group Art Unit 1632. Please make these documents of official record in U.S. Serial No. 09/433,777.**

**Respectfully submitted,**

**Thomas P. McCracken**
**Registration No. 38,548**

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*** TRANSMISSION REPORT ***

PRINT TIME 13.01.'03 18:25 ID: FAX:

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POWDERJECT PHARMACEUTICALS PLC

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| **Fax To:** | Examiner Anne Marie Sabrina Wehbe<br>United States Patent and Trademark Office<br>Group Art Unit 1632 – BOX AF |
| **Fax Nº:** | **(703) 308-4242** |
| **From:** | Thomas P. McCracken |
| **Date:** | 13 January 2003 |
| **Re:** | **Patent Application Serial No. 09/433,777** |
| **Pages:** | 3 (including this one) |

**Please deliver the attached documents (Petition for Extension of Time and Notice of Appeal), totaling with this cover sheet 3 pages, to Examiner Anne Marie Sabrina Wehbe of Group Art Unit 1632. Please make these documents of official record in U.S. Serial No. 09/433,777.**

**Respectfully submitted,**

**Thomas P. McCracken**
**Registration No. 38,548**

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**Certificate of Transmission:**
I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office, Box AF (Fax No. (703) 308-4242) on 13 January 2003 .

Printed Name: Thomas P. McCracken .

Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

HAYNES et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A.M.S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

**NOTICE OF APPEAL**

Commissioner for Patents
Box AF
Washington, D.C. 20231

Sir:

All finally rejected claims (specifically, claims 1-5, 7, 12, 15-25 and 29-47) as stated in the decision of the Primary Examiner dated 13 August 2002 are hereby appealed to the Board of Appeals.

_ Appeal Fee not required.

_ Attached is a check to cover the Appeal Fee of $320.

X Please charge the Appeal Fee of $320 to Deposit Account No. 50-0828.

X Petition for Extension of Time enclosed.

The Commissioner is hereby authorized to charge any fees under 37 CFR Sections 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0828.

Respectfully submitted,

Date: 13 January 2003

By:
Thomas P. McCracken
Registration No. 38,548

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

HAYNES et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A.M.S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

**PETITION FOR EXTENSION OF TIME**

Commissioner for Patents
Box AF
Washington, D.C. 20231

Sir:

The following extension of time is requested in order to file a response to the final Office Action mailed 13 August 2002.

X Two months to 13 January 2003. The extension fee is $410.00.

X Please charge the extension fee ($410.00) to Deposit Account 50-0828.

The Commissioner is hereby authorized to charge any fees under 37 CFR Sections 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0828.

Respectfully submitted,

Date: 13 January 2003

By:
Thomas P. McCracken
Registration No. 38,548

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Atty Dkt No. APF 18.20
PATENT

**Certificate of Deposit:**

Date of Deposit: July 8, 2003

I hereby certify that this paper and all noted attachments are being hand-deposited with the United States Patent and Trademark Office, Attn: Mail Stop RCE, on the date indicated above.

Jennifer Lohse

Typed or Printed Name of Person Depositing Paper

Jennifer Lohse

Signature of Person Depositing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

HAYNES et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A. M. S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

**REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL PURSUANT TO 35 U.S.C. §132(b) AND 37 C.F.R. §1.114**

Sir:

This is a Request for Continued Examination (RCE) under 37 C.F.R. §1.114 of the above-identified application. A Notice of Appeal was filed on 13 January 2003 in the subject application, and this request is being submitted within the extended statutory period for filing the Appeal Brief.

**1. Submission Required under 37 C.F.R. §1.114.**

a. Applicants have enclosed herewith:

i. X Response to the Final Office Action dated 13 August 2002.

ii. X Petition for Extension of Time and Fee Therefor.

iii. X Information Disclosure Statement, Form 1449, and cited references.

**2. Miscellaneous.**

a. Applicant requests limited suspension of action on the above-identified application pursuant to 37 C.F.R. §1.103 for a period of _____.

**3. Fees.**

a. The Director is hereby authorized to charge the following fees to Deposit Account No. 50-0828:

i. _X_ The RCE fee required under 37 C.F.R. §1.17(e). The RCE fee is $740.00.

ii. ___ The fee for Limited Suspension of Action pursuant to 37 C.F.R. §§1.103(c) and 1.17(i). The processing fee is _____.

b. The Commissioner is hereby authorized to charge any further fees which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0828.

Respectfully submitted,

Date: 7 July 2003

By: _____
Thomas P. McCracken
Registration No. 38,548

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**Certificate of Deposit:**

Date of Deposit: July 8, 2003

I hereby certify that this paper and all noted attachments are being hand-deposited with the United States Patent and Trademark Office, Attn: MAIL STOP RCE, on the date indicated above.

Jennifer Lohse

Typed or Printed Name of Person Depositing Paper

Jennifer Lohse

Signature of Person Depositing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

HAYNES et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A. M. S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

COMMUNICATION

Commissioner for Patents
Washington, D.C. 20231

Sir:

This is in response to the final Office Action issued in the above-identified application, that Action having been mailed 13 August 2002. This Communication is submitted with a Request for Continued Examination (RCE) and the fee therefor. Reconsideration of the application is respectfully requested in view of the following remarks.

## REMARKS

Introductory Comments:

Claims 1-26 and 29-47 were pending in the application. Claims 6, 8-11, 13-14 and 26 have been withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b) as drawn to a non-elected invention. Accordingly, claims 1-5, 7, 12, 15-25 and 29-47 are currently under consideration and were examined in the Office Action dated 13 August 2002. Applicants note with appreciation that the Office has withdrawn the following rejections: **(a)** the rejection of claims 27 and 28 under 35 U.S.C.§101; **(b)** the rejection of claims 27 and 28 under 35 U.S.C. § 112, second paragraph; and **(c)** the rejection of claims 29-32 under 35 U.S.C. §112, first paragraph.

However, the following claim rejections have been maintained: **(1)** claims 1, 16 and 33-47 remain rejected under 35 U.S.C. §112, first paragraph, as nonenabled; **(2)** claims 1, 2, 7, 12, 15, 29, 33, 35, 37, 39, 41, 43, 46 and 47 remain rejected under 35 U.S.C. § 102(e) as unpatentable over US Patent No. 5,925,362 to Spitler et al. ("Spitler"); and **(3)** claims 1, 3-5, 17-25, 29-34, 36-38, 40, 42, 44 and 45 stand rejected under 35 U.S.C. §103(a) as unpatentable over Spitler in view of Fynan et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:11478-11482 ("Fynan"), Golding et al. (1994) *Am. J. Trop. Med. Hyg.* 50(4):33-40 ("Golding"), and Sedegah et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:9866-9870 ("Sedegah"). Applicants respectfully traverse these rejections for the following reasons.

The Rejection under 35 U.S.C. §112, first paragraph:

Claims 1, 16 and 33-47 remain rejected under 35 U.S.C. §112, first paragraph, as nonenabled. Initially, the Office correctly points out that applicants have elected a single species for the current examination, that is, DNA vaccine compositions containing a lipid adjuvant composition, and that the application contains a working example of this composition, wherein CEA-encoding DNA was administered with and without the monophosphoryl lipid A (MPL) adjuvant (Example 1).. The Office's position is that, although applicants' Example 1 shows a decrease in the ratio of CEA-specific IgG1 to IgG2a in mouse sera when compared to administration of the CEA plasmid alone, this does not enable the invention as claimed since "it is clear that applicants' data does not demonstrate a 'shift' from Th2 to Th1 since the overall ratio of IgG1 to IgG2a shows that the predominant isotype is IgG1 rather than IgG2a which indicates a Th2 type response" and "applicants' data therefore only demonstrates a decrease in the magnitude of the T helper response rather than an actual shift." Office Action at page 5. On this basis, the Office concludes "it would have required undue experimentation to practice the invention as claimed." Office Action at page 7. Applicants respectfully traverse.

The single issue at hand regarding the instant enablement rejection can be summarized as being a difference between the Office's and applicants' interpretation of the data from Example 1. Applicants submit that the significant shift in the IgG1/IgG2 ratio seen with all compositions where the MPL adjuvant was co-administered with the CEA antigen-encoding DNA demonstrates a shift from a predominantly Th2 response to a Th1 response. The Office submits that the data merely show a decrease in the magnitude of the T helper response. Applicants respectfully submit that the Office has come to the wrong conclusion for the following reasons.

It is well known in the art that antibody synthesis in almost all classes shows considerable dependence upon T-cooperation. In particular, synthesis of the entire IgG class is heavily influenced by the relevant T helper response. A reduction in the T helper response would therefore affect both IgG1 and IgG2 production, presumably decreasing production of both IgG isotypes in roughly the same order of magnitude. Accordingly, if the Office's position were correct and the only result of administering the MPL adjuvant was to reduce the T helper response without bringing about a Th2/Th1 shift, one would expect to see no change in the magnitude of the IgG1/IgG2 ratio, but rather an overall change in the frequency of the humoral response. In other words, identical decreases to both the numerator and the denominator of the ratio would not reduce the ratio, for example the magnitude of the two ratios: 30,000/1000 and 30/1 are identical, it is just that in the first ratio, the frequency of the observed event was greater. However, as demonstrated in Example 1, use of the MPL adjuvant shifted the ratio of IgG1 to IgG2 in all of the experimental groups. In one case, the shift was evidenced by a decrease that was five-fold, from 27.5/1 to 4.5/1. Applicants submit that this sort of shift cannot be explained by the Office's theory of general T helper reduction, that is, it is not simply a matter of generally disabling the T helper response, it is demonstration of a significant shift in the immune response where the immune response has been shifted from one IgG isotype to another.

With regard to the Office's argument that the overall ratio of IgG1 to IgG2 continues to show the predominant isotype as IgG1 "which indicates a Th2 response" (and therefore no shift), applicants note that the Office must be arguing that in order to have a Th1/Th2 shift, one must eliminate one of the two isotypes from participating in the immune response. Applicants submit that this is not the case. As disclosed and discussed numerous times throughout applicants' specification, an immune-shift adjuvant merely "shifts" the nature of the immune response from favoring one type of

response to another. It is not a matter of eliminating the entire IgG1 response, it is a matter of significantly increasing the IgG2a component of the overall immune response. This demonstrated increase in the IgG2a component of the immune response, applicants submit, is the result of a shift from a Th1-type response to a Th2-type response, not some sort of general disabling of the T helper response.

More particularly, it is well known in the art that the cytokine interferon-gamma (IFN-γ) selectively induces switching to IgG2a in mice, and that the cytokine interleukin 4 (IL-4) reduces IgG2a production.. The two best defined subsets of helper T cells are Th1 cells which secrete IL-2 and IFN-γ, and Th2 cells which secrete IL-4. Thus, the skilled artisan understands that, when two compositions are compared head-to-head and the difference between the two test compositions is the addition of an adjuvant, and there is a marked increase in the IgG2a response as a result of the addition of the adjuvant, there has been a Th1/Th2 switch.

For all of the foregoing reasons, then, the rejection of claims 1, 16 and 33-47 under 35 U.S.C. §112, first paragraph, is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

The Rejection under 35 U.S.C. §102(e):

Claims 1-2, 7, 12, 15, 29, 33, 35, 37, 39, 41, 43, 46 and 47 stand rejected under 35 U.S.C. §102(e) as anticipated by Spitler. In particular, the Office asserts that Spitler discloses the combination of a non-DNA adjuvant and an antigen-encoding nucleic acid sequence. Applicants strongly disagree.

The Office asserts that when claims 1 and 5-7 of Spitler are read, "there can be no doubt that contemplated applicants' claimed combination of nucleic acid encoding an antigen and non-DNA adjuvant." Office Action at page 8. This is an incorrect conclusion. The subject claims of Spitler are drafted in such a way so as to cover the

various vaccine compositions that are disclosed in the Spitler specification (one cannot claim what one has not disclosed). The Office has interpreted the Spitler claims in such a way as to arrive at applicants' recited compositions, but the Office has not used the Spitler specification in order to make this interpretation, it has used applicants' specification instead. This is not permissible. One must consider the Spitler specification for what it actually disclosed to skilled artisan, where that disclosure is considered in light of the general understanding in the art at the time of applicants' filing date.

As applicants have already demonstrated in their previous response, Spitler et al. contemplated certain peptide-based vaccine compositions, and then contemplated certain DNA-based vaccine compositions. Reading the disclosure of Spitler's columns 7-8 in order (starting at the top of column 7 and ending at the bottom of column 8, one sees that Spitler et al. first considered the peptide vaccines. Next, Spitler states that liposomal compositions are preferred (generally). Spitler then switches to a specific discussion of just a certain embodiment of their invention, where liposomal formulations incorporating the prostate antigens (that is, protein antigens) may also include adjuvants. See column 7, line 47 through column 8, line 2 of Spitler. Never once does Spitler mention, suggest, describe or even so much as hint that a DNA vaccine composition may contain an adjuvant. The reason for this was simple. This combination would not have made sense to Spitler et al., nor to any other ordinarily skilled artisan without access to applicants' disclosure. This is because the skilled artisan knew and understood that for a DNA vaccine to work, the subject nucleic acid had to both gain entry into a suitable host cell cytoplasm and gain entry into the host cell nucleus where DNA could then be transcribed. Failure to get the DNA all the way into the nucleus meant failure of the vaccine since no antigen would be expressed. However, at the same time, the skilled artisan knew and

understood that adjuvants exerted their effect in the extracellular spaces of tissue. That is, lipids, proteins, saponins, alum salts and the like would not be expected to have the desired adjuvant effect if they were delivered into the nucleus of a cell. What use would it be to deliver alum into a cell nucleus? The lipid compositions described by Spitler would not be expected, for example, to be smart enough to spit out the adjuvant component prior to entry into the cell and cell nucleus, after which it would then spit out the DNA component. Accordingly, without the benefit of applicants' teaching, the skilled artisan would not combine the DNA vaccine with a non-DNA form adjuvant in a liposome as suggested by the Office. This is why when Spitler et al. discuss incorporation of adjuvants in a liposome composition, they were very careful to limit their discussion to compositions containing the prostate antigen (in protein form).

What the Office has done is to combine applicants' disclosure with the Spitler disclosure and then arrive at applicants' recited invention. When the Spitler claims are read in light of the Spitler disclosure and in light of the knowledge and understanding of the skilled artisan--without benefit of applicants' disclosure--it is clear that Spitler never contemplated combining a DNA vaccine with a non-DNA adjuvant. Claim 1 of Spitler provides two choices, protein or DNA vaccine compositions. Claim 5 of Spitler picks up certain optional compositions that contain an adjuvant. The correct reading of the Spitler specification teaches that these certain optional, adjuvant-containing compositions are always protein antigen vaccines, not DNA vaccines. Claims 6 and 7 of Spitler merely recite particular adjuvants. The Office's attention is drawn to the fact that the list of adjuvants recited in claim 7 of Spitler are taken from the Spitler specification that specifically recites that when the vaccine contains a protein antigen, they can be combined with certain adjuvants (column 7, line 47 through column 8, line 2 of Spitler).

Anticipation of a claim under §102 *requires* that each and every element of the claims be inherent in, or disclosed expressly by the anticipating reference. *Constant v. Advanced Micro-Devices, Inc.*, 7 USPQ2d 1057, 1064 (Fed. Cir. 1988). Exclusion of a single claimed element from a prior art reference is enough to negate anticipation by that reference. *Atlas Powder Co. v E.I. du Pont De Nemours & Co.* 224 USPQ 409, 411 (Fed. Cir. 1984). Further, anticipation basically requires identity with the prior art document *(Tyler Refrigeration v. Kysor Indus. Corp.*, 227 USPQ 845 (Fed. Cir. 1985)), where the identical invention must be shown in as complete detail as is contained in the rejected claim (*Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913 (Fed. Cir. 1989)). Finally, in order to anticipate, a prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public. *Akzo N.V. v. United States ITC*, 1 USPQ2d 1241 (Fed. Cir. 1986).

Spitler clearly fails to anticipate applicants' recited invention since it does not provide any disclosure whatsoever regarding applicants' recited combination of nucleic acid and non-DNA components. Since Spitler never even contemplated such a combination, the reference cannot be considered to be enabling, thus placing the allegedly disclosed matter in the possession of the public. Applicants submit that the Office's rejection is based upon an incorrect reading of Spitler, where portions of the specification dealing with peptide/protein antigen compositions has been incorrectly combined with other sections of the specification that deal with DNA compositions that encode an antigen. The only way to arrive at the Office's proposed interpretation of Spitler is to use applicants' disclosure as prior art. This is clearly not permissible.

For all of the foregoing reasons, then, the rejection of claims1-2, 7, 12, 15, 29, 33, 35, 37, 39, 41, 43, 46 and 47 under 35 U.S.C. §102(e) is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

The Rejection under 35 U.S.C. §103(a):

Claims 1, 3-5, 17-25, 29-34, 36-38, 40, 42 and 42-45 stand were rejected under 35 U.S.C. §103(a) as unpatentable over Spitler in view of Fynan, Golding and Sedegah. In particular, the Office relies upon Spitler as the primary reference for the same reasons as discussed in the Section 102 rejection, and then combines this with the secondary references to find gene gun delivery techniques (Fynan), use of a malaria antigen (Sedegah) and use MPL as an immune shift adjuvant (Golding). The Office again asserts that claims 1 and 5-7 of Spilter "clearly recite the combination of an expression system encoding PSA antigen and a non-adjuvant such as MPL." Office Action at Page 10. Applicants respectfully traverse.

Section 2143 of the M.P.E.P. sets forth the following three basic requirements for *prima facie* obviousness: (1) there must be some suggestion or motivation to modify or combine the references; (2) there must be a reasonable expectation of success for the modification and/or combination; and (3) the prior art reference must teach or suggest all the claim limitations. When assessing these issues, (1) the claimed invention must be considered as a whole; (2) the references must be considered as a whole and must suggest the desirability of making the combination; (3) the references must be viewed without the benefit of impermissible hindsight; and (4) a reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 229 USPQ 182, 187, n.5 (Fed. Cir. 1986). Applicants submit that the Office has failed to satisfy these criteria, and has thus failed to establish *prima facie* obviousness over its proposed combination.

More particularly, as demonstrated above, the primary reference (Spitler) fails to teach or even so much as suggest that a non-DNA adjuvant should be combined with, e.g., a DNA encoding antigen in a single composition. The Spitler claims that the Office has relied upon must be read in light of both the specification and the general knowledge and skill in the art. In addition, applicants' disclosure does not form part of the prior art, and the Office cannot depend upon applicants' own teaching in order to support its' rejection.

As demonstrated herein above, Spitler carefully taught the skilled person that adjuvants could be added to certain compositions, when the antigen was in the protein form. This is exactly in line with the knowledge and skill possessed by the ordinarily skilled artisan who would not have combined a DNA vaccine with a non-DNA adjuvant in a liposome as suggested by the Office due to the expectation that these two components must be delivered to entirely different areas in order to exert their desired effect. The Office has taken applicants' disclosure and then used it to interpret the Spitler claims and disclosure in such a way that Spitler et al. never intended and in fact were careful to exclude. This is an impermissible hindsight reconstruction of the prior art, and is not properly based on the cited prior art. Applicants note that when a modification to (or combination of) a prior art disclosure would render that prior art inoperative (based on the understanding of the ordinarily skilled artisan), such a modification is improper.

Accordingly the Office's assertion that Spitler et al. somehow teach a DNA vaccine composition combined with a non-DNA adjuvant is not based on a proper reading of the Spitler claims and disclosure. It is based in its entirety on applicants' own disclosure. The secondary references to Fynan, Golding and Sedegah likewise fail to teach such a novel combination, and the Office has not asserted otherwise. Accordingly, the rejection fails to teach or suggest all of applicants' recited claim

limitations. Since the cited prior art fails to teach or suggest applicants' recited combination compositions, there cannot have been a reasonable expectation for success for such compositions. Accordingly, the Office has failed to establish a *prima facie* showing of obviousness over its proposed combination since the proposed combination and each component thereof fails to teach or suggest all of applicants' recited claim limitations. Accordingly, the rejection of claims 1, 3-5, 17-25, 29-34, 36-38, 40, 42 and 42-45 under 35 U.S.C. §103(a) is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

## CONCLUSION

Applicants respectfully submit that the claims as now pending define an invention which complies with the requirements of 35 U.S.C. § 112 and which is novel and nonobvious over the art. Accordingly, allowance is believed to be in order and an early notification to that effect is earnestly solicited. Applicants further ask that, should the Examiner note any minor remaining issues that may be resolved with a telephone call, that he contact the undersigned in the UK at +44 1865 332 600.

Respectfully submitted,

Date: 7 July 2003

By: _____
Thomas P. McCracken
Registration No. 38,548

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Oxford OX4 4GA
United Kingdom
Telephone: +44 1865 332 600
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Atty Dkt: APF 18.20
PATENT

**Certificate of Deposit:**

Date of Deposit: July 8, 2003

I hereby certify that this paper and all noted attachments are being hand-deposited with the United States Patent and Trademark Office, Attn: Mail Stop RCE, on the date indicated above.

Jennifer Lohse

Typed or Printed Name of Person Depositing Paper

Jennifer Lohse

Signature of Person Depositing Paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Haynes et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A.M.S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

**INFORMATION DISCLOSURE STATEMENT**
**UNDER 37 C.F.R. § 1.97(b)**

Commissioner for Patents
Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. Copies of the information and completed PTO-1449 forms are

submitted herewith. The Examiner is respectfully requested to make this information of official record in the application. The information includes:

United States Patent No. 5,630,796 issued May 20, 1997 to Bellhouse et al.;
United States Patent No. 4,945,050 issued July 30, 1990 to Sanford et al.;
United States Patent No. 5,100,792 issued March 31, 1992 to Sanford et al.;
United States Patent No. 5,120,657 issued June 9, 1992 to McCabe et al.;
United States Patent No. 5,149,655 issued September 22, 1992 to McCabe et al.;
United States Patent No. 5,204,253 issued April 20, 1993 to Sanford et al.;
United States Patent No. 5,584,807 issued December 17, 1996 to McCabe;
United States Patent No. 5,589,466 issued December 31, 1996 to Felgner et al.;
United States Patent No. 5,630,496 issued May 20, 1997 to Bellhouse et al.;
United States Patent No. 5,738,852 issued April 14, 1998 to Robinson et al.;
United States Patent No. 5,865,796 issued February 2, 1999 to McCabe;
United States Patent No. 6,168,587 issued January 2, 2001 to Bellhouse et al.;
United States Patent No. 6,194,389 issued February 27, 2001 to Johnston et al.;
International Publication No. WO 94/24263, published October 27, 1994;
International Publication No. WO 95/19799, published July 27, 1995;
International Publication No. WO 96/04947, published February 22, 1996;
International Publication No. WO 96/12513, published May 02, 1996;
International Publication No. WO 96/14855, published May 23, 1996;
International Publication No. WO 96/20022, published July 04, 1996;
International Publication No. WO 97/32987, published September 12, 1997;
International Publication No. WO 97/48485, published December 24, 1997;

International Publication No. WO 98/10750, published March 19, 1998;

International Publication No. WO 98/46263, published October 22, 1998;

International Publication No. WO 99/27961, published June 10, 1999;

International Publication No. WO 00/12121, published March 09, 2000;

International Publication No. WO 00/13704, published March 16, 2000;

Haynes J R, "Genetic Vaccines," *Infectious Disease Clinics Of North America.* 13(1):11-26 (1999);

Sasaki et al., "The Search for a Potent DNA Vaccine against AIDS: The Enchancement of Immunogenicity by Chemical & Genetic Adjuvants", *Anticancer research* 18:3907-3916 (1998);

Sasaki et al., "Monophosphoryl Lipid A Enchances Both Humoral & Cell-Mediated Immune Responses to DNA Vaccination against Human Immunodeficiency Virus Type 1", *Infection & immunity.* 65(9):3520-3528 (1997);

Lodmell et al., "DNA Vaccination of mice aginst rabies virus: effects of the route of vaccination and the adjuvant monophosphoryl lipid A (MPL)" *Vaccine.* 18:1059-1066 (2000); and

Pow & Crook, "Extremely high titre polyclonal antisera against small neurotransmitter molecules: rapid production, Characterisation and use in light-and electron-microscopic immunocytochemistry", *J. of Neuroscience Methods.* 48:51-63 (1993).

This Information Disclosure Statement under 37 CFR § 1.97(b) is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the

information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

By: _____
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Registration No. 38,548

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Atty Dkt No. APF 18.20

COMMISSIONER OF PATENTS AND TRADEMARKS999
Washington, D.C. 20231

FORM PTO-1449 (Modified)
LIST OF PATENTS AND PUBLICATIONS
FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT
(Use several sheets if necessary)
Sheet 1 of 3

In the Application of Haynes et al.

Serial No.: 09/433,777

Art Unit: 1632

Filed: 3 November 1999

Examiner: A.M.S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

U.S. PATENT DOCUMENTS

| Exam. Init. | Ref. Desig. | Document No. | Date | Name | Class | Sub Class | Filing Date |
|---|---|---|---|---|---|---|---|
| | AA- 1 | 4,945,050 | July 30, 1990 | Sanford et al. | | | |
| | AB- 1 | 5,100,792 | March 31, 1992 | Sanford et al. | | | |
| | AC- 1 | 5,120,657 | June 9, 1992 | McCabe at al. | | | |
| | AD- 1 | 5,149,655 | September 22, 1992 | McCabe et al. | | | |
| | AE- 1 | 5,204,253 | April 20, 1993 | Sanford et al. | | | |
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Examiner: Date Considered:

EXAMINER: Initial if citation considered whether or not the citation conforms with MPEP609. Draw a line through the citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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In the Application of Haynes et al.

Serial No.: 09/433,777

Art Unit: 1632

Filed: 3 November 1999

Examiner: A.M.S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

FOREIGN PATENT DOCUMENTS

| Exam. Init. | Ref. Desig. | Document No. | Publication Date | Country or Patent Office | Class | Sub Class | Translation YES | Translation NO |
|---|---|---|---|---|---|---|---|---|
| | AM-1 | WO 94/24263 | October 27, 1994 | PCT | | | | |
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FORM PTO-1449 (Modified)
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In the Application of Haynes et al.

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Title: ADJUVANTED GENETIC VACCINES

OTHER DOCUMENTS (including Author, Date, Journal, Volume, Pertinent Pages, etc.)

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In Re Application of:

HAYNES et al.

Serial No.: 09/433,777 Art Unit: 1632

Filing Date: 3 November 1999 Examiner: A. M. S. Wehbe

Title: ADJUVANTED GENETIC VACCINES

**PETITION FOR EXTENSION OF TIME**

Commissioner for Patents
Mail Stop RCE
Washington, D.C. 20231

Sir:

The following extension of time is requested pursuant to 37 C.F.R. §1.136. A Notice of Appeal was filed in the above-identified application on 13 January 2003.

X Four months to 13 July 2003. The extension fee is $1,450.00.

X Please charge the extension fee ($1,450.00) to Deposit Account 50-0828.

The Director is hereby authorized to charge any fees under 37 CFR Sections 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0828.

Respectfully submitted,

Date: 7 July 2003

By: _____
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Registration No. 38,548

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